BARBITURATES

IN VETERINARY PRACTICE

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BARBITURATES IN VETERINARY PRACTICE

For the

Veterinary Profession

BARBITURATES
IN VETERINARY PRACTICE

PHARMACEUTICAL SPECIALITIES (MAY & BAKER) LTD.

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Pharmacology of Barbiturates

THE action of drugs of the barbituric acid series is essentially one of depression of the central nervous system.

Localisation of barbiturates in the central nervous system has been demonstrated by numerous studies.

Although the action on the central nervous system is the essential one in the production of therapeutic effect, other functions of the body may be affected directly or indirectly by large doses. The following effects are among those described: a fall in body temperature, slight slowing of the basal metabolism which increases with the depth of narcosis, respiratory depression, temporary lowering of the blood pressure on rapid injection, some depression of the activity of unstriped muscle, and, under certain conditions, hyperglycæmia.

Numerous reports indicate that the barbituric acid derivatives are excreted in the urine in varying amounts, only traces being found in the fæces.

A large number of compounds of this series has been introduced into therapeutics. They vary in the intensity and duration of their actions, and are used for a variety of purposes—hypnotic, anti-spasmodic, narcotic, general anæsthetic. The duration of action of the various members of the group depends upon the extent and rapidity of their metabolism and largely determines the marked differences in their pharmacological actions.

Toxic action of Barbiturates.

Toxic effects may result from the cumulative action of therapeutic doses or through accidental over-dosage. Marked over-dosage usually results in a fall of blood pressure, depressed respiration, diminished reflexes and coma.

Treatment consists of keeping the patient warm, evacuating the stomach contents and the administration of large doses of strychnine or picrotoxin.

Death is produced either by paralysis of the respiratory centre or is due to bronchopneumonia following the production of prolonged coma.

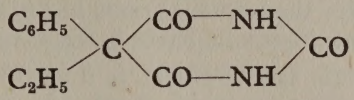
Contra-indications.

The use of barbiturates is contra-indicated in cases of marked renal or hepatic impairment or serious cardiac disorder.

Gardenal

Phenobarbitone

GARDENAL is phenylethylmalonylurea and has the following structural formula :—



It is a white crystalline powder with a somewhat bitter taste which is almost insoluble in water, but is readily absorbed from the intestinal tract, and is rapid in action following oral administration.

The sodium salt—GARDENAL SODIUM—is readily soluble, but in aqueous solution slowly decomposes on keeping. GARDENAL SODIUM for injection is, therefore, supplied in a special organic solvent in which it remains stable.

GARDENAL, in medicinal doses, has a powerful and sustained sedative effect on the central nervous system without affecting the medullary centres, so that respiration and blood pressure are not affected. It is rapidly absorbed by the intestinal tract and slowly excreted by the kidneys.

Indications.

GARDENAL is employed for its sedative and anti-spasmodic effects in the common epileptiform convulsions of dogs. In this condition its effect is soon apparent and under treatment the fits become less severe, are of shorter duration and occur at longer intervals and when the drug is gradually withdrawn there may be no return of the symptoms.

In chorea GARDENAL frequently produces a marked diminution in the spasms and considerable general improvement results. In the treatment of this condition anti-spasmodic treatment by means of GARDENAL may, with advantage, be combined with the use of STOVARSOL as a tonic.

GARDENAL is valuable for the symptomatic treatment of the nervous forms of distemper, and in cases of meningitis its effect is frequently striking.

In hysteria GARDENAL is a useful sedative. In eclampsia the drug is also of value in overcoming the tetanic spasms of the muscles, and may be used in association with other treatment, such as the injection of soluble calcium salts.

GARDENAL has been found to have an action antagonistic to strychnine. A definite complex of constant chemical composition results from the mixing of solutions of strychnine and phenobarbitone, which results in a reduction of the toxicity of the two components.

It has been found that in the dog the lethal dose of strychnine was counteracted by one-third of the lethal dose of phenobarbitone. A similar action was also seen with cocaine and other similarly acting drugs, and the use of GARDENAL is, therefore, indicated in cases of poisoning by strychnine, cocaine or their derivatives or compounds, or as a prevention of poisoning when these substances are used therapeutically.

Administration and Dosage.

GARDENAL is supplied in tablets of gr. ½ or gr. 1 for oral administration. In cases where oral administration is difficult GARDENAL SODIUM may be used by hypodermic injection in the same doses. Each

1 c.c. of GARDENAL SODIUM solution contains gr. 3 of the drug.

The following doses are suggested :—

Dogs up to 20 lb. body weight	.	grain $\frac{1}{4}$ to $\frac{1}{2}$
Dogs 20 to 30 lb. body weight	.	grain $\frac{1}{2}$ to 1
Dogs 30 to 40 lb. body weight	.	grain 1 to 2
Dogs over 40 lb. body weight	.	grain 2 to 4
Cats	.	Up to $\frac{1}{2}$ grain

These doses may be administered two or three times daily or more frequently if required and even larger doses may be indicated in some cases.

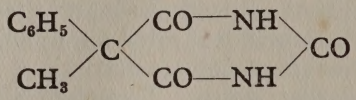
GARDENAL should preferably be administered between meals and it is advisable to begin treatment with an adequate dose and continue by means of slightly smaller doses. Treatment should not be stopped suddenly, but should be progressively reduced as improvement takes place.

For packages please refer to page 20.

Rutonal

Methophenobarbital

RUTONAL is phenylmethylmalonylurea or phenylmethylbarbituric acid. It differs from GARDENAL (phenobarbitone) in having a methyl group in place of an ethyl group, as shown by the structural formula :—



RUTONAL is a white crystalline powder, odourless and of slightly bitter taste. It is very slightly soluble in water and more soluble in alcohol, especially on warming.

It is allied in its pharmacological effects to phenobarbitone and has a sedative effect on the central nervous system without affecting the medullary centres when given in ordinary doses. It is readily absorbed by the intestinal tract and slowly excreted by the kidneys without causing irritation.

Compared to phenobarbitone it has been found in clinical practice that RUTONAL appears, weight for weight, to have an activity in the order of half that of the latter and to be less than half as toxic. Coutière (1932) found that in rabbits RUTONAL possessed a higher therapeutic index than phenobarbitone.

Indications

RUTONAL is employed as an anti-convulsant, anti-spasmodic and sedative. Its indications for

use are similar to those for GARDENAL and include the treatment of epileptiform convulsions, eclampsia, tetany, chorea and all nervous states in small animals. RUTONAL may be employed where the use of phenobarbitone has resulted in symptoms of intolerance or where the normal response to the latter has not been obtained. It may also be tried in cases where the use of phenobarbitone over a period of time has resulted in loss of control of the hind limbs. A change of drug may possibly eliminate this undesirable effect.

Dosage

The doses of RUTONAL required for sedative or anti-spasmodic effect are approximately double those used for GARDENAL. RUTONAL is supplied in tablets of grain ½ for oral administration.

Dogs under 20 lb. body weight .	grain ½ to 1
Dogs 20 to 30 lb. body weight .	grain 1 to 1½
Dogs 30 to 40 lb. body weight .	grain 2 to 3
Dogs over 40 lb. body weight .	grain 4 to 6
Cats	grain ½

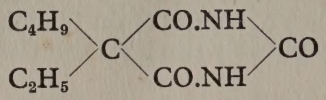
These quantities may be increased to produce more powerful effects and the administration should be repeated two or three times daily or as appears indicated by the symptoms.

For packages please refer to page 20.

Soneryl

Butobarbital

SONERYL is N-butylethylmalonylurea of the following structural formula :—



SONERYL is a white crystalline powder, melting at 123° C. It is odourless with a slightly bitter taste and is only very slightly soluble in water.

Its sodium salt, SONERYL SODIUM, is readily soluble in water and is somewhat more rapid in action than SONERYL itself.

Pharmacology

SONERYL is a powerful hypnotic which is rapid in action and quickly eliminated. Carnot and Tiffeneau (1922) studied the hypnotic effect of N-butylethylmalonylurea and its sodium salt in the dog by three routes of administration—oral, intravenous and subcutaneous. A few cgms. injected intravenously produced sound and lasting sleep. Taken by the mouth, a quantity only slightly larger had the same effect. A dose of 5 cgms. per kgm. produced sleep for 20 to 30 minutes.

SONERYL is almost completely detoxicated by the tissues within a few hours and there is no danger of cumulative toxic effects.

Indications.

SONERYL may be used in dogs and cats where a rapidly acting sedative or hypnotic is required—*e.g.*,

in hysteria and other nervous states; also for pre- or post-operative medication, to allay nervousness when travelling or following accidents, etc.

SONERYL SODIUM, on account of its more rapid and somewhat more profound hypnotic effects, is indicated as a basal narcotic, prior to the induction of anæsthesia by chloroform or ether, also for carrying out minor operations, with or without additional local anæsthesia, and it is a useful narcotic for use in euthanasia.

Administration and Dosage

SONERYL is supplied in the form of tablets of grain 1½ for oral administration. The following doses may be given :—

Dogs under 20 lb. body weight .	½ to 1 tablet
Dogs 20 to 30 lb. body weight .	1 to 2 tablets
Dogs 30 to 40 lb. body weight .	2 to 4 tablets
Dogs over 40 lb. body weight .	4 to 6 tablets
Cats	Up to 1 tablet

These doses may be repeated two or three times daily as required.

SONERYL SODIUM is supplied in capsules containing 0.15 Gm. (gr. 2¼). These capsules may be given by mouth or when used prior to destruction the dose may be dissolved in water to make a 10 per cent. solution and given by intraperitoneal or intravenous injection. For this purpose double the recommended doses may be used.

Dosage of SONERYL SODIUM

Dogs under 25 lb. body weight: ⅓ grain per lb. body weight (approx. 1½ capsules per 10 lb. body weight).

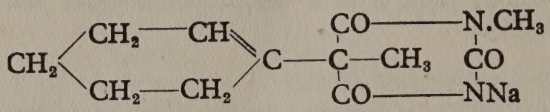
Dogs over 25 lb. body weight and aged animals: ¼ grain per lb. body weight (approx. 1 capsule per 10 lb. body weight).

For packages please refer to page 20.

Cyclonal Sodium

Hexobarbitone Soluble

CYCLONAL SODIUM is the sodium compound of N-methyl-C-C-cyclohexenyl-methylmalonylurea and has the following graphic formula :



It is a white crystalline powder, very soluble in water, affording a clear solution. The solution is not stable for more than two or three hours.

It is available in ampoules of 0.50 gramme, together with an appropriate quantity of distilled water.

To prepare the solution the distilled water, previously warmed, should be added to the contents of the dry ampoule and solution is brought about by drawing the contents into the syringe and expelling two or three times. Solutions must be prepared as required. A 10 per cent. solution is generally used and anæsthesia is produced very rapidly on intravenous injection.

Pharmacology

The therapeutic index for cats has been stated to be 4, 25 mgms. per kgm. giving full anæsthesia, while the lethal dose was from 100 to 110 mgms. In dogs the quotient was found to be 3.3. Perfusion experiments on the dog's heart have shown that the drug has no depressant effect. Rapid intravenous injection causes a fall in blood pressure with, how-

ever, quick recovery. If the solution is injected slowly the pulse remains regular and full. There is no significant effect on the blood sugar level and but little effect on body metabolism. The solution is non-irritant to tissues when injected subcutaneously or intraperitoneally.

Applications

CYCLONAL SODIUM has found extensive use in human surgery for the production of short anæsthesia by intravenous injection and has been found remarkably safe.

Dogs.—Auchterlonie (1934) published his experiences with Hexobarbitone Soluble in 14 cases in dogs, and expressed complete satisfaction with its action for operations of short duration. Prenarcotization by means of papaveretum and scopolamine was adopted.

Wright (1938) stated that he had tried the drug in canine surgery, but found that the period of recovery was associated with great excitement, and for this reason it was discarded. This writer considers that its anæsthetic potency is about one-half that of Pentobarbital sodium (sodium ethyl-l-methyl-butyl-barbiturate) and of sodium-ethyl-l-methyl-butyl-thio-barbiturate. At the same time its action is not as transient as in man and narcosis persists for several hours.

It has been suggested that the tendency to excitement may be diminished by prenarcotization of the animal prior to the induction of anæsthesia and also by injecting the solution warmed to body temperature.

Not infrequently this drug causes muscular tremors in dogs under anæsthesia.

Dosage

For anæsthesia in dogs a dose of approximately 0.10 Gm. per 5 lb. body weight is used in the form of a 10 per cent. solution in distilled water, administered by intravenous injection. It appears, however, that owing to the struggling and excitement during the recovery period that the drug is only suitable as an anæsthetic agent in canines when methods for preventing this can be applied.

CYCLONAL SODIUM is very useful for the production of general anæsthesia before destruction, and for this purpose double the ordinary anæsthetic dose may be given.

For packages please refer to page 20.

References

1. Auchterlonie, L.A. (1934), *Vet. Rec.*, **14**, 21.
2. Carnot, P., and Tiffeneau, M. (1922), *C.R. Acad. Sc.*, Vol. 175, 1922, p. 241.
3. Coutière, J. (1932), "De la détermination des Constantes de toxicité et d'activité de quelques Dérives de la Série Barbiturique."—*These de Paris.*
4. Wright, J. (1938), *Vet. Rec.*, **49**, 27, and *Medical Press and Circular*, May 4th, 1938.

Supplies

* GARDENAL

Containers of 50 × gr. ½ tablets	. . . .	1/6
„ 250 × gr. ½ „	. . . .	5/6
„ 1000 × gr. ½ „	. . . .	19/6
„ 250 × gr. 1 „	. . . .	8/0
„ 1000 × gr. 1 „	. . . .	29/3

* GARDENAL SODIUM

Boxes of 6 × 1 c.c. ampoules of solution (each c.c. containing gr. 3)	. . . . .	3/0

* RUTONAL

Containers of 50 × gr. ½ tablets	. . . .	2/0
„ 250 × gr. ½ „	. . . .	9/6

* SONERYL

Containers of 50 × gr. 1½ tablets	. . . .	4/9
„ 250 × gr. 1½ „	. . . .	21/0

* SONERYL SODIUM

Containers of 50 × 0.15 Gm. capsules	. . .	9/0
„ 250 × 0.15 Gm. „	. . .	40/0

* CYCLONAL SODIUM

1 × 0.50 Gm. ampoule with distilled water	. .	1/9

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